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Case Report

A huge gluteal mass diagnosed as CIC-rearranged sarcoma: a rare case report and literature review

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Abstract: Capicua transcriptional repressor (CIC)-rearranged sarcoma, also known as CIC-rearranged sarcoma (CRS), is a recently recognized sarcoma subtype characterized by specific molecular features. It is associated with aggressive clinical course and a poor prognosis. Here, we present a rare case of CRS, including a detailed clinical, pathological, and molecular analysis, to enhance understanding of this disease and provide a reference for future diagnosis and treatment. A 15-year-old female adolescent initially presented with a rapidly growing mass in her left buttock, accompanied by intermittent pain. A magnetic resonance imaging (MRI) scan revealed a 12.7 × 8.6 × 11.9 cm mixed-intensity mass, suggesting a mesenchymal sarcoma. After histological and immunohistochemical analysis, a preliminary diagnosis of malignant small round cell tumor was made, which was later confirmed as CRS by Fluorescence in situ hybridization (FISH). A course of VDC/IE regimen was administered as first-line neoadjuvant chemotherapy. However, a follow-up MRI showed a 28% increase in tumor volume. Given the poor response to chemotherapy, we decided to perform a wide resection surgery. Unfortunately, lung metastases developed only one month postoperatively, and local recurrence occurred two months postoperatively. The patient then underwent concurrent chemoradiotherapy. At the time of data cutoff, the patient achieved a stable disease state and retained satisfactory walking function. In conclusion, treatment paradigms for CRS have yet to be defined. For patients with large tumor volumes, preoperative neoadjuvant chemotherapy may be ineffective and could potentially delay more effective treatment. Early surgical resection is probably a more suitable treatment option. Multidisciplinary collaboration is essential in the treatment of CRS, and large studies exploring novel therapeutic options are urgently needed to bring hope to patients with this aggressive disease.

Keywords: Capicua (CIC)-rearranged sarcoma (CRS), mesenchymal sarcoma, wide resection surgery, chemotherapy, radiotherapy

Introduction

The Capicua (CIC) gene functions as a tumor suppressor. It contains a high-mobility group (HMG) box, which recognizes specific DNA sequences, thereby regulating the expression of various target genes. It plays a crucial role in regulating transcription and cell proliferation by acting as a negative regulator of the mitogen-activated protein kinase (MAPK) signaling pathway. This pathway is often associated with cellular processes such as invasion and proliferation, which are pivotal to the development and progression of various cancers [1].

CIC-rearranged sarcoma, previously recognized as an Ewing-like sarcoma characterized by an undifferentiated small round cell sarcoma without the specific FET::ETS gene fusions typical of Ewing sarcoma (ES), is an extremely rare type of soft tissue sarcoma. This tumor entity belongs to the translocation-associated sarcomas, which was established by Kawamura-Saito, et al. in 2006 when they identified CIC::DUX4 fusion transcripts in two Ewing-like sarcomas with the t(4;19)(q35;q13) translocation [2]. After fusion with other genes, most commonly DUX4 (in 95% of cases), the transcriptional repressor CIC converts to an oncogene that can promote tumor growth and metastasis. Unlike Ewing sarcoma, CIC-rearranged sarcomas are associated with an aggressive clinical course and a poor prognosis.

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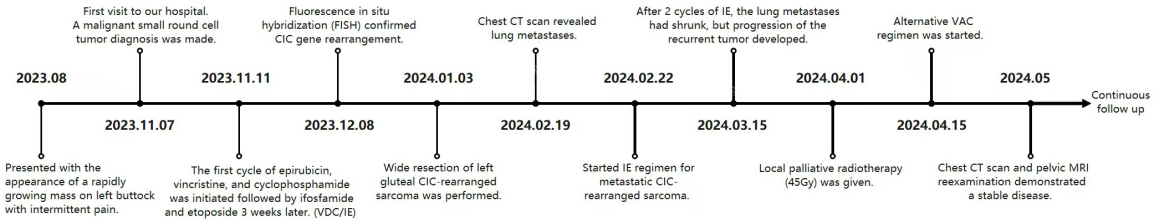

Figure 1. Summary of the clinical course.

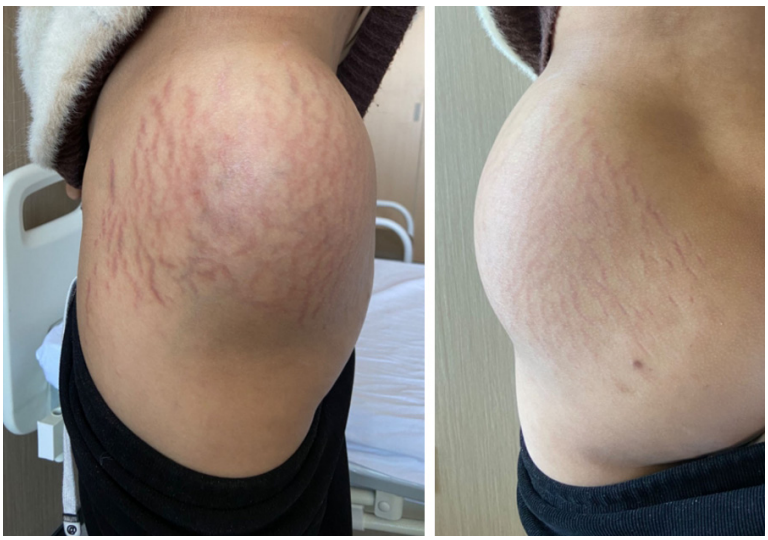

Figure 2. Gross view of the tumor at presentation.

CIC-rearranged sarcomas most commonly present in young adults and typically originate from soft tissues of extremities. They often manifest as a lump that gradually increases in size, with or without pain. The clinical symptoms are related to the location of tumor occurrence. Generally, to achieve a precise diagnosis, a combination of pathology, immunohistochemistry and molecular testing is required, including CIC break-apart FISH analysis, to confirm the presence of specific fusion transcripts involving CIC [3]. With the development of genetic testing, nowadays reverse transcription polymerase chain reaction (RT-PCR) and next-generation sequencing (NGS) are also widely used [2]. At diagnosis, about 40% of patients found metastases to lungs or lymph nodes, which indicates the highly aggressiveness of this disease. Currently, there is still no optimal treatment strategy. Due to the similarity in pathological properties, patients with CIC-rearranged sarcomas are commonly treated in the same way as Ewing sarcoma, which combines neoadjuvant and adjuvant anthracycline-based polychemotherapy regimen, surgery, and radiotherapy. However, the response is often poor comparing with ES, especially for patients in advanced stage. The 5-year overall survival rate ranges from 17% to 43%, and the median survival is 12 to 18 months [2, 4, 5]. Due to the extreme rarity of this disease, clinical studies are encountering enrollment difficulties and suffer from a lack of investment, resulting in most of them being stuck in the preclinical stage. Thus, to explore an effective, evidence-based therapeutic strategy, more and more clinical data is needed.

Herein, we report a case of a 15-year-old patient with CIC-rearranged sarcoma originating from the left buttock. The tumor developed rapidly and, after surgery, it metastasized to the lungs. Subsequently, local recurrence occurred. After standardized treatment according to guidelines, the patient achieved a stable disease state. During the hospital course, informed consent was obtained from the patient's parents for the inclusion of their child's medical data, clinical images, and any associated information in this study. The parents were provided with detailed information about the study's purpose, procedures, potential risks, and benefits. The parents have given their full consent for the publication of their child's de-identified medical information and images, with the assurance that all identifiable information has been removed to protect the child's privacy. The clinical course is summarized in **Figure 1**.

Clinical presentation

In November 2023, a 15-year-old female adolescent with no significant medical history pre-

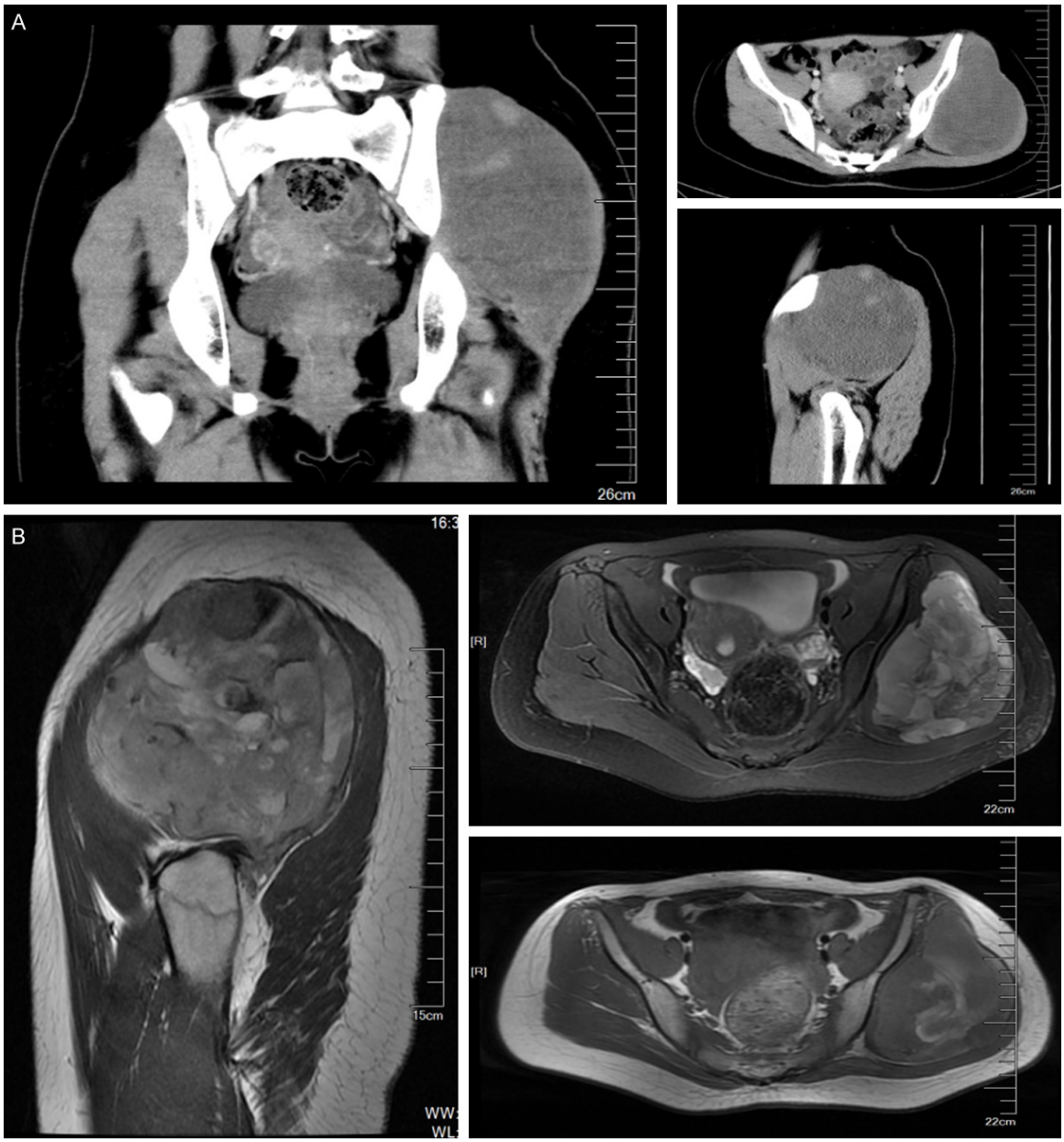

Figure 3. A. CT images of the tumor at presentation in coronal, transverse and sagittal position, showing a huge mass originating from gluteal region. No evidence of invasion into the surrounding bone was observed. B. T1-weighted and T2-weighted imaging with fat suppression MR images of the tumor indicated heterogeneous enhancement. The tumor was located deep in the gluteus maximus muscle.

sented with a rapidly growing mass on her left buttock, accompanied by intermittent pain over the previous three months. A magnetic resonance imaging (MRI) scan of the left buttock, taken prior to referral, revealed a left gluteal mass, suggesting mesenchymal sarcoma. She underwent a needle biopsy before being referred to our department, which revealed the presence of small round cells. Upon physical examination, a solid mass, approximately 13 × 15 cm in size, was observed on the left buttock. The presence of multiple red streaks on the skin surface indicated the rapid growth of the tumor (**Figure 2**). The mass was in hard consistency with tenderness on palpation and its boundary was not clear. Muscle strength and skin sensation of the left lower limb was not impaired. The movement of the left hip joint

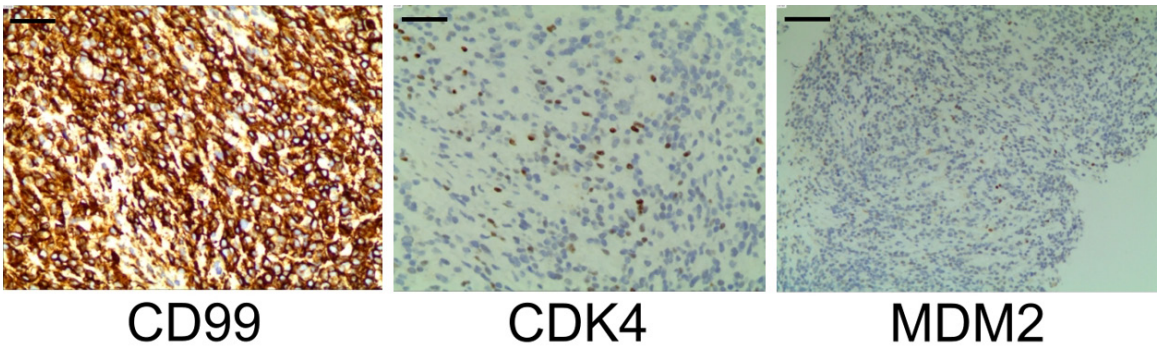

Figure 4. Immunohistochemical studies demonstrated multifocal positivity for CD99 (magnification, ×200; scale bar = 100 μm), and focal expressions for CDK4 (magnification, ×200; scale bar = 100 μm) and MDM2 (magnification, ×100; scale bar = 100 μm).

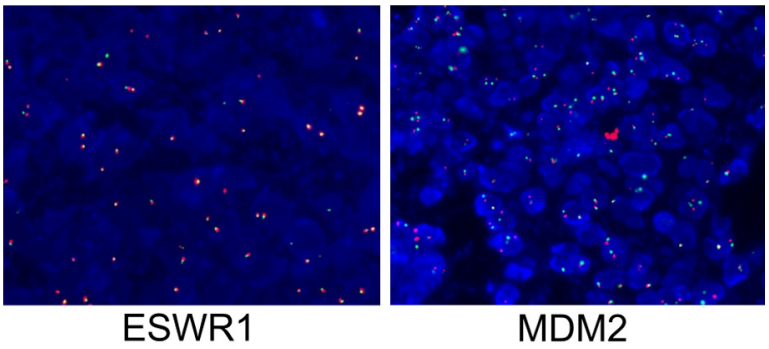

Figure 5. The Fluorescence in situ hybridization (FISH) assay did not detect any breakage in the ESWR1 or MDM2 genes (magnification, ×1,000).

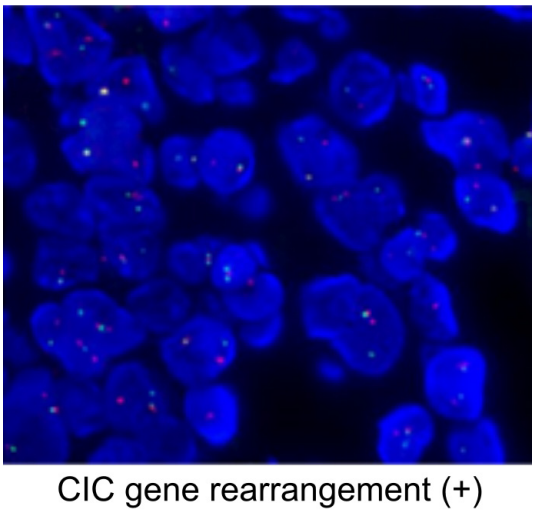

Figure 6. FISH analysis confirmed CIC gene rearrangement (magnification, ×1,000; the red and green dots in the nucleus represent gene rearrangement).

was not restricted. Besides, no enlargement of lymph nodes was palpitated in both groins. CT scan showed a low-density with patchy high-density mass originating from gluteus medius muscle, approximately 130 mm × 90 mm in size (**Figure 3A**). On MRI, both T1 and T2 weighted images showed mixed intensities, and the tumor was heterogeneously enhanced (**Figure 3B**). Immunohistochemical examination was conducted on the specimen obtained from a previous biopsy. The results demonstrated positivity for CD99, Vimentin (Vim), H3K27me3, and Ki67 (with 60% positivity), as well as focal expression of CDK4 and MDM2 (**Figure 4**). In contrast, no expression was observed for the following markers: CK, CD30, ALK, MyoD1, MUM1, Myogenin, SS18-SSX, TFE3, TdT, SATB2, or S100. Furthermore, genetic analysis demonstrated negative results for Ewing sarcoma breakpoint region 1 (EWSR1) gene detection and MDM2 gene amplification (**Figure 5**). Based on these findings, the initial diagnosis was a malignant small round cell tumor, suspected to be either Ewing sarcoma or a CIC-rearranged sarcoma. Subsequently, the specimen was sent for FISH analysis.

Since the neoadjuvant chemotherapy regimen is essentially the same for malignant small round cell tumors, following a multi-disciplinary evaluation, we decided to start first-line neoadjuvant chemotherapy with cyclophosphamide, doxorubicin, and vincristine in alternation once every 3 weeks with ifosfamide and etoposide (VDC/IE). To reduce cardiac toxicity, we substituted epirubicin for doxorubicin. The first cycle

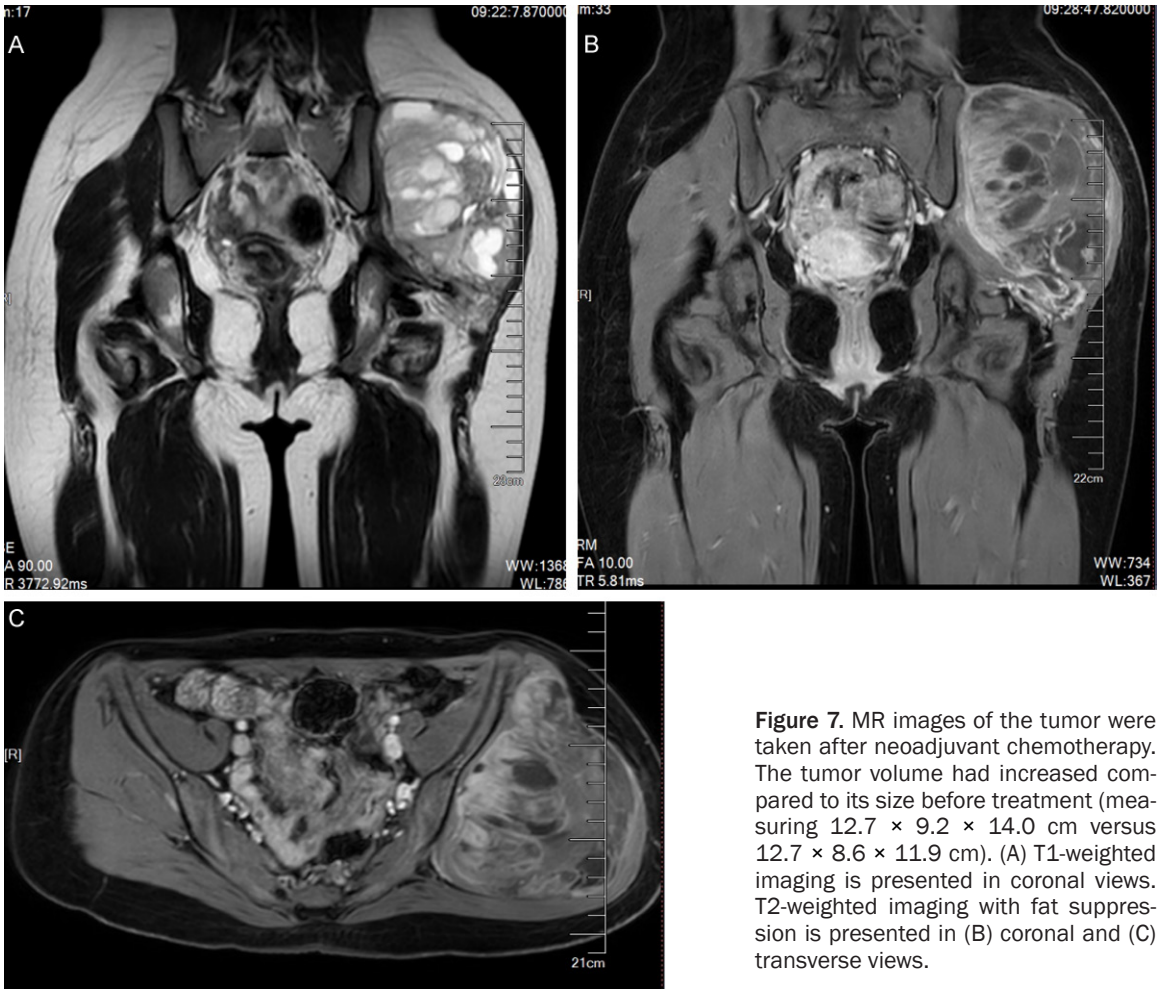

Figure 7. MR images of the tumor were taken after neoadjuvant chemotherapy. The tumor volume had increased compared to its size before treatment (measuring 12.7 × 9.2 × 14.0 cm versus 12.7 × 8.6 × 11.9 cm). (A) T1-weighted imaging is presented in coronal views. T2-weighted imaging with fat suppression is presented in (B) coronal and (C) transverse views.

of epirubicin, vincristine, and cyclophosphamide began on November 11, 2023. During this cycle, the patient experienced grade 2 anorexia and nausea. Three weeks later, we administered ifosfamide and etoposide. On December 8th, FISH analysis confirmed CIC gene rearrangement (**Figure 6**), but the fusion partner was not identified. Combining with previous findings, a final diagnosis of a CIC-rearranged sarcoma was made.

After treatment, the pain in the left buttock was alleviated. However, a follow-up MRI showed that the tumor volume in the left buttock had increased by 28%, with more pronounced enhancement of the solid components (**Figure 7**). Considering the unsatisfactory effects of neoadjuvant chemotherapy, after careful discussion among the multidisciplinary team and with the patient's family, a wide resection surgery was planned. This surgery aimed to reduce tumor load and to obtain gross specimens for a precise pathological diagnosis.

On January 3rd, 2024, wide resection of the left gluteal mass, including fascia and the underlying gluteus medius and minimus muscles, was performed. A rectangular incision was made along the left femoral trochanter, the left iliac crest, the posterior superior iliac spine to the gluteal groove, surrounding the initial biopsy site (**Figure 8A**, **8B**). After flipping the rectangular skin flap, the tumor was fully revealed and removed. To remove the tumor, the origin site of gluteus medius and minimus muscles was separated from the ilium (**Figure 8C**) and superior and inferior gluteal nerve and blood vessels were ligated. Subsequently, below the tumor, the insertion sites of gluteus medius, gluteus minimus and piriformis muscle were separated from the left greater trochanter. The tumor was completely removed from front to back after

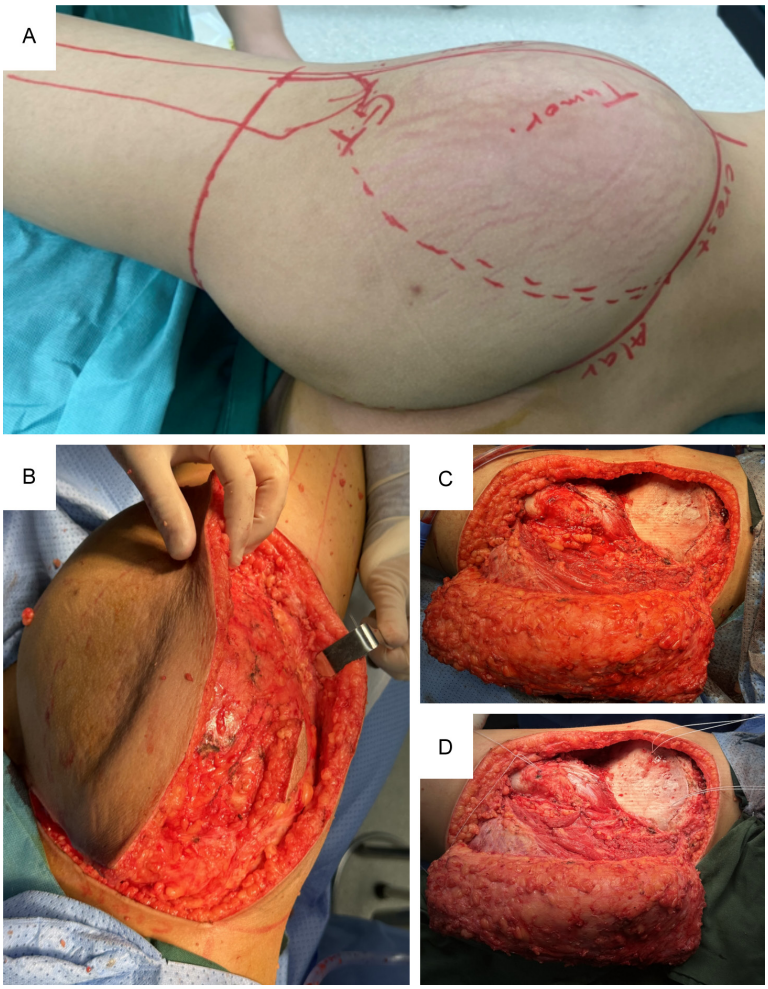

Figure 8. Photos taken during surgery are as follows. A. The patient was positioned in a lateral decubitus position. B. A rectangular incision was made around the initial biopsy site. C. After the rectangular skin flap was flipped, the tumor was fully revealed and subsequently removed. D. Soft tissue reconstruction was performed using non-absorbable anchor sutures.

cutting down part of the gluteus maximus posterolaterally to ensure adequate negative margins. During the procedure, the sciatic nerve was carefully protected. Next, soft tissue reconstruction was performed, which is an essential step to maintain optimal motor function of lower limbs postoperatively. A non-absorbable anchor nail was implanted at the greater trochanter, and the gluteus maximus and piriformis muscles were fixed to it. The fascia layer was sutured and fixed on the ilium by two anchor nails implanted to reduce dead space (**Figure 8D**). The incision was closed layer by layer after thorough hemostasis and irrigation. Four drainage tubes were placed, and systemic antibiotics are used to prevent local infection. Intraoperative blood loss was about 500 ml. A blood transfusion consisting of 1.5 units (U) of red blood cells and 200 milliliters (ml) of fresh frozen plasma (FFP) was administered.

Pathological findings

Grossly, a huge, round-shape mass was obtained, measuring 15.0 × 13.0 × 7.0 cm. The cut surface of this tumor has a soft, fish-flesh-like appearance, ranging from white to tan and yellow, with areas of regional bleeding and necrosis (**Figure 9**). Histological analysis showed that the tumor was composed of small to medium-sized blue round cells with sparse cytoplasm and obvious nucleoli (**Figure 10**). Immunohistochemically, it was noted to be positive for CD99 and focally positive for WT1 and S100 (**Figure 11**). No expression of CK, SALL4, SATB2, NUT, Desmin and LCA was observed. Combined with the results of genetic testing, a diagnosis of CIC-rearranged sarcoma was confirmed, with the classification of ypT-3N0M0, stage IIIB.

Follow up and postoperative treatment

After the surgery, the wound healing was satisfactory, and the patient was able to walk without support two weeks postoperatively. However, she experienced mild claudication because the extension, abduction and external rotation of the left hip joint were limited following the removal of most of the gluteal muscles. Because the tumor is highly malignant, postoperative adjuvant therapy was strongly recommended. To investigate possible treatment alternatives like targeted therapy and immunotherapy, a detailed genetic test was conducted using next-generation sequencing technology (NGS). However, gene variations related to targeted drugs recommended by FDA approval and NCCN guidelines, including BRAF, RET, NTRK1, NTRK2, and NTRK3, were not detected. The homologous recombination repair gene (HRR) variation test was negative, suggesting that the

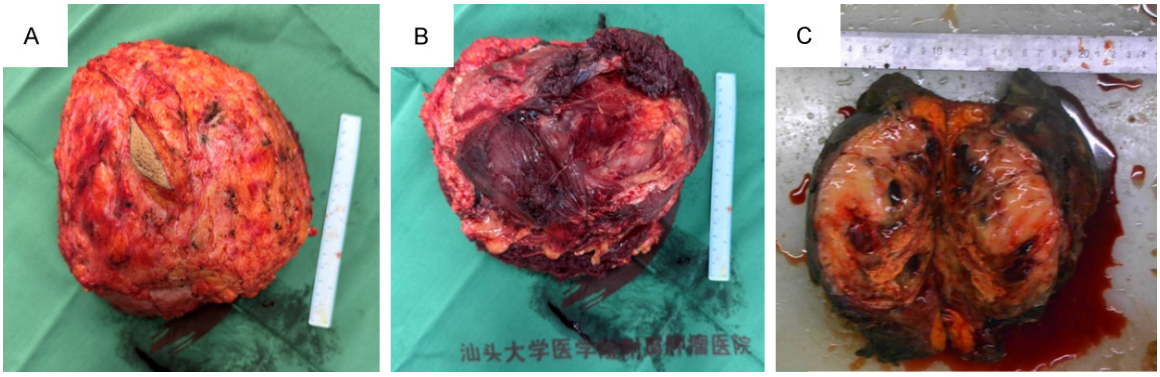

Figure 9. The gross view of the resected tumor from three perspectives. (A) The front, (B) the back and (C) the cut surface.

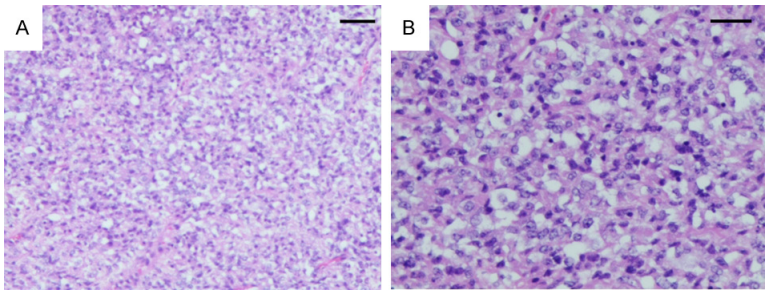

Figure 10. HE staining preparation showed diffuse and tumorous growth of small round cells with sparse and transparent cytoplasm, and fine chromatin in the nucleus. A. Magnification, ×100; scale bar = 100 μm. B. Magnification, ×200; scale bar = 50 μm.

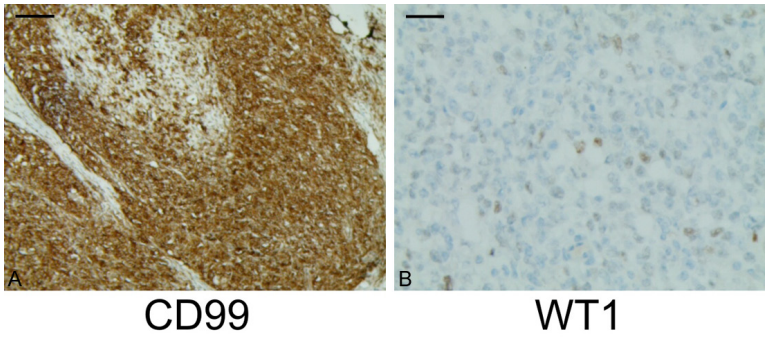

Figure 11. A. Diffuse nuclear staining for CD99 was present in postoperative FISH assay (magnification, ×200; scale bar = 100 μm). B. WT1 was focally positive (magnification, ×200; scale bar = 100 μm).

patient may not benefit from PARP inhibitor therapy. Tumor mutation burden (TMB) result is TMB-L (0.00 Muts/Mb), indicating a poor response to immune checkpoint inhibitors (**Figure 12**). Additionally, the PD-L1 test result was CPS<1, indicating that the patient may not benefit from PD-1/PD-L1 immune checkpoint inhibitor treatment. This test also covered genes related to angiogenesis, such as FLT1, FLT3, KDR, and VEGFA, but no mutations or amplifications were detected, which means the angiogenesis signal did not show any enhancement or weakening at the DNA level. However, anti-angiogenic drugs such as bevacizumab, sorafenib, sunitinib, apatinib, lenvatinib, anlotinib, and regorafenib may still be suitable for this patient. Based on these findings, following a multi-disciplinary discussion, we decided to perform traditional chemotherapy combined with radiotherapy to control tumor progression.

The patient returned to our department for further treatment on February 19th, 2024. On pelvic CT scan, an irregular, encapsulated fluid accumulation was observed in the surgical area and a nodular lesion was seen near the left piriformis muscle, measuring approximately 1.9 × 2.7 cm, with inhomogeneous enhancement and blurred edges, indicating a local tumor recurrence (**Figure 13**). Chest CT scan revealed multiple nodules in the lungs, consistent with metastases (**Figure 14A**). No other distant metastatic lesions were found. On February 22nd, we administered ifos-

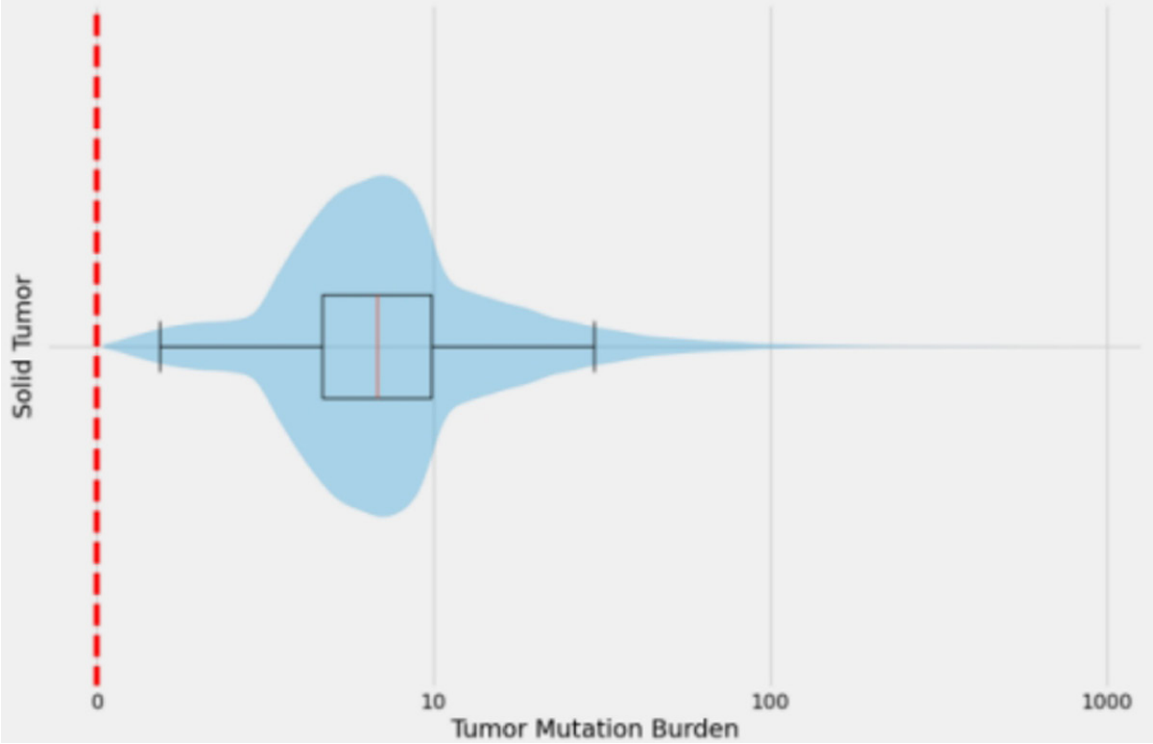

Figure 12. Tumor mutation burden (TMB) result is TMB-L (0.00 Muts/Mb).

famide and etoposide, in combination with a 5-HT3 receptor antagonist, NK1 receptor antagonist, and dexamethasone, to prevent vomiting. After two cycles of the IE regimen, the lung metastases had shrunk (**Figure 14B**, **14C**), but progression of the recurrent tumor was observed (**Figure 15**). Subsequently, concurrent chemoradiotherapy was conducted. Local palliative radiotherapy (45 Gy) was initiated on April 1, 2024, after confirming good wound healing (**Figure 16**), and the VAC regimen was started on April 11, 2024. The subsequent chest CT scan and pelvic MRI demonstrated stable disease (**Figure 17**). At the time of data cutoff, the patient remains without evidence of tumor progression on continued surveillance imaging. Despite a slight limp, walking was not limited upon discharge.

Discussion

CIC-rearranged sarcoma (CRS) is a novel subtype of sarcoma that was included in the fifth edition of the World Health Organization (WHO) Classification of Tumors of Soft Tissue and Bone in 2020. This sarcoma subtype is characterized by specific molecular rearrangements involving the CIC gene, leading to distinct pathological and clinical features. CRS is often challenging to diagnose due to its overlapping morphological features with other sarcoma subtypes, particularly Ewing sarcoma. In addition, most tumors have a predilection for occurring in soft tissue, with 87% of cases found there. The most frequent primary tumor locations are the limbs, followed by the trunk, and the head and neck region [4]. However, there are only a few cases reported in the gluteal region. Here, we report a case of CRS, including a detailed clinical, pathological, and molecular analysis, and we also conduct a literature review to compare this case with previously reported ones, with a particular focus on cases where tumors occurred in the gluteal region (**Table 1**).

Traditionally, the diagnosis of CIC-rearranged sarcomas has relied heavily on histological assessment and immunohistochemical analysis. However, these methods can be challenging due to the overlapping morphological features with other sarcoma subtypes. Moreover, immunohistochemical markers lack specificity and sensitivity, further complicating the diagnostic process. Previous studies have reported

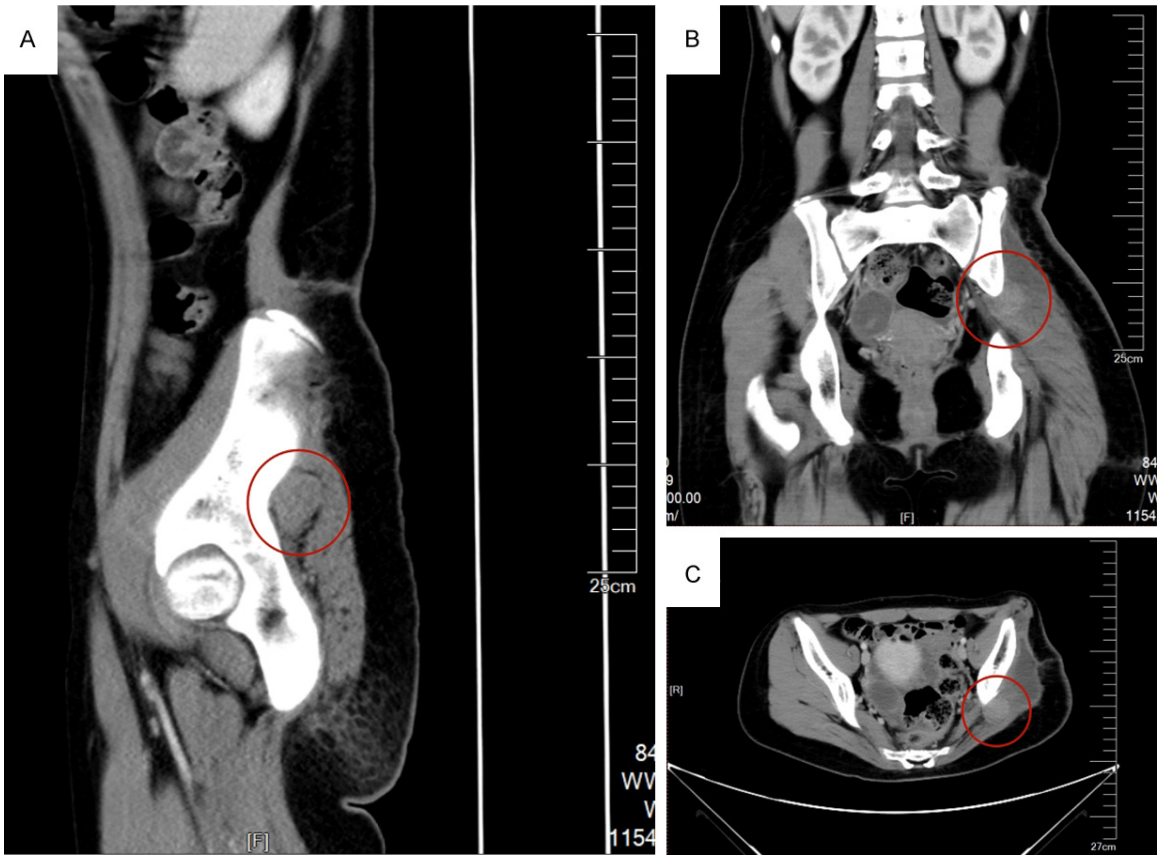

Figure 13. Pelvic CT scans taken one month after the surgery, presented in (A) sagittal, (B) coronal, and (C) transverse views, revealed a nodular lesion near the left piriformis muscle, noted with a red cycle, measuring 1.9 × 2.7 cm, indicating a local tumor recurrence.

that the majority of CIC-rearranged sarcomas test positive for CD99. In addition, nuclear WT1 positivity is observed in 70% to 95% of these cases [4]. Other proposed positive markers include the NUT protein, which is expressed by CIC::NUTM1 sarcoma. Labeling for S100 protein, desmin, and synaptophysin is rare [2]. In this case, we performed immunohistochemistry both preoperatively and postoperatively. The results all showed CD99 positivity, and we found focally positive for WT1 and S100 postoperatively, which is consistent with previous reports. The expression of S100 protein confirmed the diversity of immunophenotypes of CRS. However, the definitive diagnosis relies on the identification of a CIC gene rearrangement. In recent years, molecular diagnostics, including fluorescence in situ hybridization (FISH), reverse transcription-polymerase chain reaction (RT-PCR), and next-generation sequencing (NGS) technologies, have emerged as more precise tools for detecting CIC gene rearrangements. FISH is more commonly used due to minimal sample requirements and faster results. Moreover, once the presence of CIC fusions is detected, a diagnose of CRS can be made even if the partner gene is unknown. However, it is reported that 14% to 25% of cases produce negative signal patterns despite the presence of CIC fusions [10], which means it is not highly sensitive. Nowadays, there are novel diagnostic approaches developing with a promising future, such as targeted multiplexed next-generation sequencing (NGS)-based method, which utilizes ligation dependent reverse transcriptase polymerase chain reaction (LD-RT-PCR-NGS) to detect oncogenic fusion transcripts [11] and AI-assisted analysis, which integrates AI and machine learning algorithms into diagnostic workflows [12]. As we continue to unravel the molecular complexities of this disease, the integration of these novel

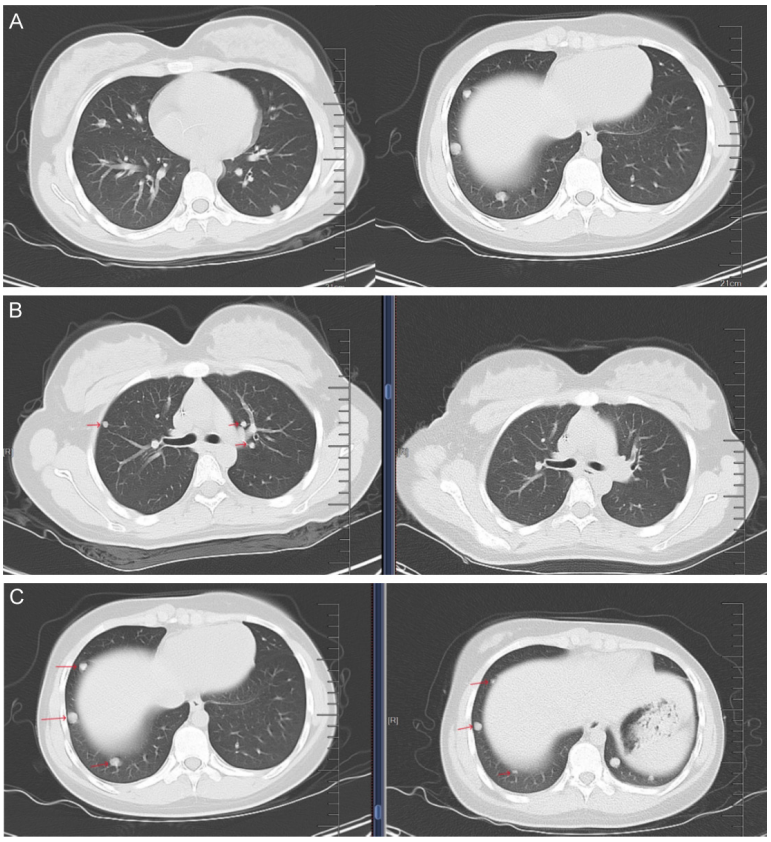

Figure 14. A. Chest CT scan at different levels revealed multiple nodules in the lungs, which were consistent with metastases. B. After two courses of adjuvant chemotherapy, the lung metastases had shrunk, with the largest nodule measuring approximately 0.8 cm and exhibiting clear edges. The nodules in the lungs, indicated with red arrows, had disappeared. Left panel: Chest CT scan taken on Feb 19, 2024. Right panel: Chest CT scan taken on Mar 15, 2024. C. The nodules in the lower lungs, noted with red arrows, had shrunk. Left panel: Chest CT scan taken on Feb 19, 2024. Right panel: Chest CT scan taken on Mar 15, 2024.

diagnostic tools into clinical practice will undoubtedly improve patient outcomes and guide the development of targeted therapies.

It is known that CIC-rearranged sarcomas appear to be less chemo-sensitive than Ewing sarcomas [2, 3, 7, 9]. In this case, the disease was localized at the time of referral, and we performed neoadjuvant chemotherapy using an Ewing sarcoma regimen. The result was poor tumor control, which is consistent with previous reports [4]. Considering that the efficacy of chemotherapy in the localized setting is unclear and delayed resection may increase the metastatic risk, Connolly EA et al. proposed initial resection rather than neoadjuvant therapy [7]. We immediately switched to surgical treatment upon discovering tumor progression, but lung metastases developed only one month later after surgery. It is reported that a sustained response to systemic treatment seems limited in advanced diseases. In most studies, patients received treatment with multiagent Ewing-based chemotherapy, most commonly VDC/IE. Other non-cytotoxic therapies like tyrosine kinase inhibitors (regorafenib, pazopanib) and immunotherapy (pembrolizumab) were tried but showed poor response [3]. Novel treatment methods, such as specific inhibitors targeting some of the CIC-DUX4-related interactors are still under exploration. Due to the rarity of the disease and thus lack of interest from Big Pharma, the development of new treatments still requires a considerable amount of time. In this case, after MDT (Multi-Disciplinary Team) discussion, we initiated IE regimen for palliative treatment and the shrinkage of lung metastases was found after 2 cycles of IE, which is in line with the report from Kimbara S et al. [13], which achieved a good response in lung metastases lasting for four months.

However, local recurrence occurred only two months after the surgery. Concurrent chemoradiotherapy was conducted to enhance local control. In a cohort study reported by Connolly EA et al. [7], radiotherapy was undertaken postoperatively in 6 patients (mean 58 Gy in 30 fractions) of whom two developed local (and distant) recurrence. Chebib I et al. [6] described a 69-year-old woman who presented with a 9-month history of left hip pain and a left gluteal mass. She received radiotherapy (49.75 Gy over 25 fractions) without complications and demonstrated symptomatic improvement; restaging scans revealed primary tumor shrinkage. In our practice, we observed a stable disease period lasting for one month, which may support the efficacy of concurrent chemoradiotherapy. Unfortunately, due to poor economic conditions, the patient declined subsequent treat-

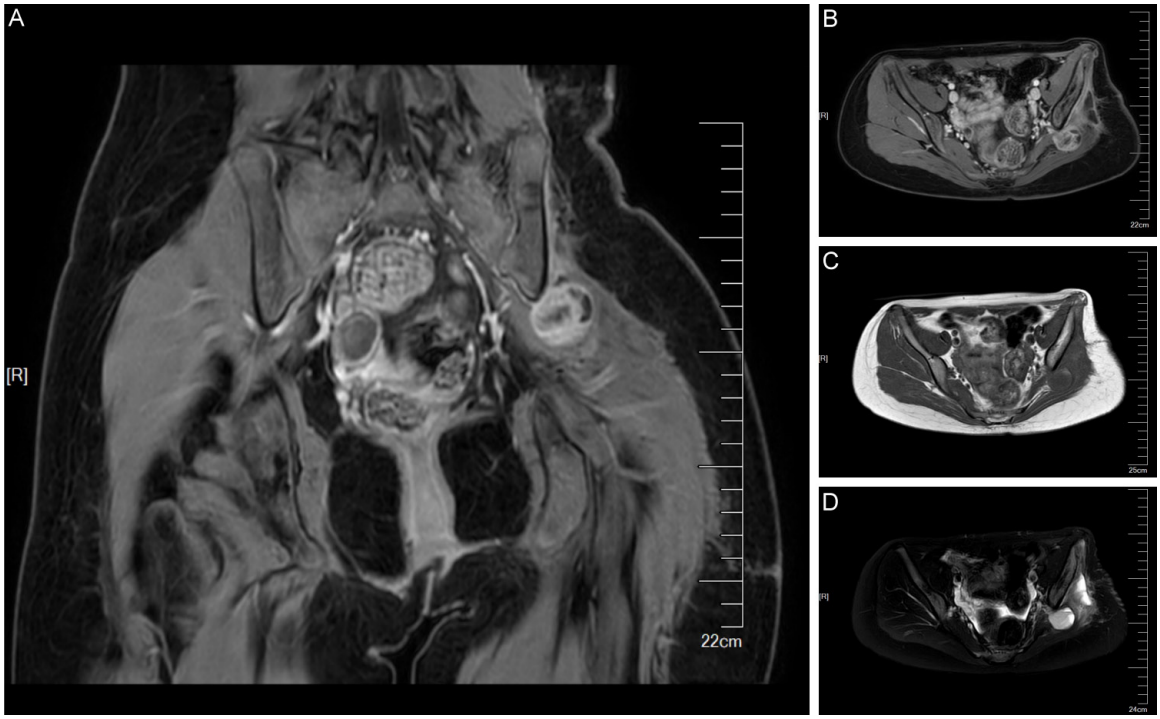

Figure 15. Pelvic MRI after adjuvant chemotherapy revealed a nodular mass, approximately 32 × 25 mm in size, located between the deep surface of the gluteal muscle and the piriformis muscle in the left buttock. The mass has unclear boundaries and shows no invasion of the left iliac bone. T2-weighted imaging with fat suppression is presented in (A) coronal and (B) transverse views. (C) T1-weighted imaging is presented in transverse views. (D) The enhancement sequence is also included.

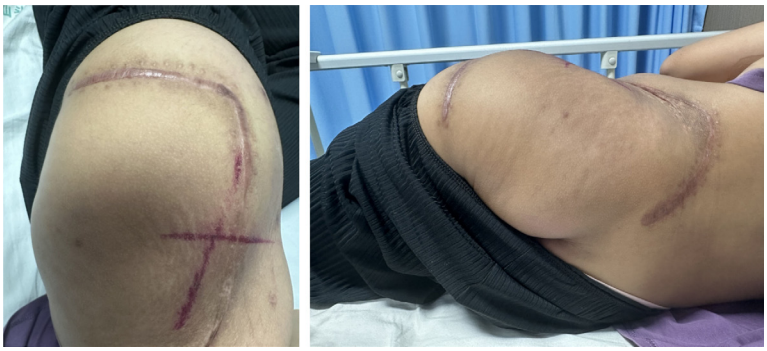

Figure 16. Photos taken three months postoperatively show good wound healing.

ment. The prognosis for this patient is not optimistic given that median overall survival (OS) was only 12.6 months in those presenting with advanced disease [7]. In a case series including 10 patients with CIC-rearranged sarcoma treated at the Johns Hopkins Hospital reported by Murphy J et al. [9], a 17-year-old male presented with an 18.3 cm left buttock mass and died 18 months after initial diagnosis despite receiving multimodal treatments similar to our case. Furthermore, they found that patients with a tumor size of less than 5 cm experienced a significant survival advantage compared to those presenting with primary tumors larger than 5 cm at diagnosis.

In the past five years, we have observed remarkable growth in clinical trials and laboratory work to explore targeted therapy and immunotherapy for bone and soft tissue sarcomas (STSs). Consequently, we explored possibilities of other treatment protocols in this case by conducting genetic testing. The results showed that CPS<1 and the TMB (Tumor mutation burden) test result was TMB-L (0.00 Muts/Mb), suggesting that the patient may not benefit from PD-1/PD-L1 immune checkpoint inhibitor therapy. This finding aligns with the previous research of

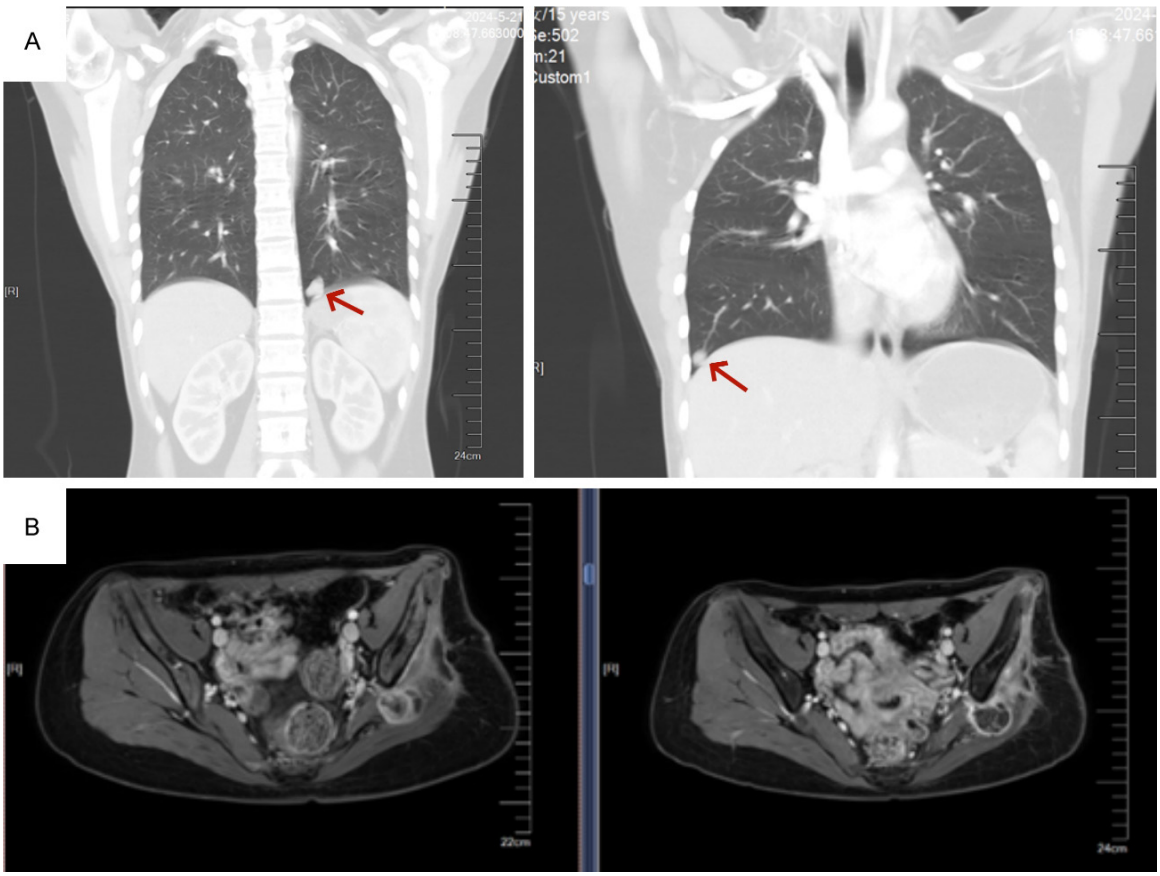

Figure 17. Follow-up examination images. A. A chest CT scan performed on May 21st revealed multiple metastatic tumors, indicated with red arrows, in both lungs. Some tumors showed shrinkage, while others demonstrated an increase in size compared to previous scans. B. An MRI indicated that the size of the tumor remains essentially the same as before, but the enhancement has been reduced. The two panels display different layers of the tumor as observed on MRI scans.

Moreno Tellez C et al. [14], who noted that the majority of sarcomas are immunologically "cold", with sparse immune infiltration. The lack of immune responses may depend on the genetic background, as sarcomas often have a low TMB or are driven by translocations, potentially limiting neoantigens available for immune responses. In addition, no gene variations related to targeted drug use were detected. From our review of the reported data, early experiences treating CRS with pazopanib, pembrolizumab and trabectedin have been disappointing, and most research into potential molecular targets remains in a preclinical phase. There is an urgent need for large studies on novel therapeutic options to offer hope to patients with a poor prognosis.

Conclusion

Our case report confirms that CIC-rearranged sarcoma is a rare tumor type characterized by high malignancy and strong invasiveness. To achieve a precise diagnosis, a combination of pathology, immunohistochemistry, and molecular testing is required, with a particular emphasis on CIC break-apart FISH analysis. For patients with large tumor volumes, preoperative neoadjuvant chemotherapy is likely to be ineffective and may even delay treatment. Therefore, for such patients, early surgical resection may be a more appropriate treatment option, although there is still a risk of local recurrence after surgery. This disease typically has a poor prognosis, and there is a lack of consensus on the best treatment plan, necessitating multidisciplinary collaboration and further studies of novel treatment protocols. This study was limited by the short follow-up period, and further research is warranted to better characterize the long-term tumor control after multimodal treatments for CIC-rearranged sarcomas. Despite its limitations, this article broadens the

Table 1. CIC-rearranged sarcomas reported in the gluteal region in existing literature

Source	Age (years)/ Gender	Primary tumor site, size (cm)*	Metastases at diagnosis	Chemotherapy	Radiotherapy	Surgery	Immunohistochemistry Characteristics	Outcome
Chebib I and Jo VY, [6] 2016	69/F	Left buttock, 8.7	Numerous bilateral, subcentimeter pulmonary nodules	Doxorubicin (4 cycles); IT	49.75 Gy, 25 fractions	No	Positive: CD99, WT1 Negative: Cytokeratin, EMA, S100, glial fibrillary acidic protein, SOX-10, Desmin, CD34	PD after 4 cycles of doxorubicin
Connolly EA et al., [7] 2022	34/M	Gluteus, 2.7	No	No (declined treatment)	No	R0 excision	Positive: CD99 Negative: Not mentioned	NED, 37.3 months after initial diagnosis
Faden DF et al., [8] 2024	23/M	Left buttock nodule with ulceration, 11	No	VDC/IE (adjuvant)	No	R0 excision	Positive: MDM2, vimentin, WT1, and CD99 Negative: S100, SOX-10, AE1/3, Pan Cytokeratin, SMA, ERG, CD3, CD45, PAX-5, CD138, Desmin, NSE, P63, HHV8, and EBV	NED, 14 months after initial diagnosis
Murphy J et al., [9] 2024	17/M	Left gluteus maximus, 18.3	2 external iliac lymph nodes	VDC/IE (neoadjuvant and adjuvant)	Neoadjuvant IMRT, 45 Gy, 25 fractions	R0 excision	Positive: CD99, 013, TLE1, ERG, CD68, EMA; retained BAF47 and INI1 Negative: AE1, AE3, S-100, Desmin, SMA, myogenin, HMB45, CD3, CD20, TdT, keratin	DOD, 18 months after initial diagnosis

Abbreviations: F, female; M, male; IT, irinotecan, temozolomide; VDC, vincristine, doxorubicin, and cyclophosphamide; IE, ifosfamide, etoposide; IMRT, Intensity-Modulated Radiation Therapy; Gy, grey; R0, microscopic complete resection; PD, progressive disease; NED, no evidence of disease; DOD, dead of disease. *size denotes the largest single dimension of the tumor at the time of diagnosis.

scope of reported clinical outcomes and provides valuable additions to the published literature on this rare cancer.

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Disclosure of conflict of interest

None.

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